

What is claimed is:

1. A medical device comprising:

an interventional component to be deployed in a patient;

a beneficial agent to be delivered from the interventional component, the beneficial

5 agent loaded on at least a portion of the interventional component and having a first LogP value; and

an effective amount of a hydration inhibitor associated with the beneficial agent to control delivery of the beneficial agent from the interventional component, the hydration inhibitor having a second LogP value, the second LogP value being greater than the first

10 LogP value.

2. The device according to claim 1, wherein the beneficial agent is selected from a group consisting of antithrombotics, anticoagulants, antiplatelet agents, anti-lipid agents, thrombolytics, antiproliferatives, anti-inflammatories, agents that inhibit hyperplasia, smooth  
15 muscle cell inhibitors, antibiotics, growth factor inhibitors, cell adhesion inhibitors, cell adhesion promoters, antimetotics, antifibrins, antioxidants, antineoplastics, agents that promote endothelial cell recovery, antiallergic substances, viral vectors, nucleic acids, monoclonal antibodies, antisense compounds, oligonucleotides, cell permeation enhancers, pro-drugs and combinations thereof.

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3. The device according to claim 2, wherein the beneficial agent is selected from the group of indomethacin, phenyl salicylate, B-estradiol, vinblastine, ABT-627, testosterone, progesterone, paclitaxel, cyclosporin A, vincristine, carvedilol, vindesine, dipyridamole, methotrexate, folic acid, thrombospondin mimetics, estradiol, dexamethasone, metrizamide,  
25 iopamidol, iohexol, iopromide, iobitridol, iomeprol, iopentol, ioversol, ioxilan, iodixanol, iotrolan and pro-drugs, analogs, derivatives, or combinations thereof.

4. The device according to claim 2, wherein the beneficial agent is a nucleic acid that encodes a pharmaceutically useful peptide or an anti-sense oligo-nucleotide used to control a  
30 gene of interest in a cell of the patient.

5. The device according to claim 1, wherein the hydration inhibitor is selected from a group consisting of beneficial agents, polymeric materials, markers, additives, and combinations thereof.

5           6. The device according to claim 1, wherein the hydration inhibitor is a second beneficial agent.

7. The device according to claim 6, wherein the second beneficial agent is selected from a group consisting of antioxidants, antithrombotics, anticoagulants, antiplatelet agents, anti-lipid agents, thrombolytics, antiproliferatives, anti-inflammatories, agents that inhibit hyperplasia, smooth muscle cell inhibitors, antibiotics, growth factor inhibitors, cell adhesion inhibitors, cell adhesion promoters, antimitotics, antifibrins, antioxidants, antineoplastics, agents that promote endothelial cell recovery, antiallergic substances, viral vectors, nucleic acids, monoclonal antibodies, antisense compounds, oligonucleotides, cell permeation enhancers, radiopaque agents markers and combinations thereof.

8. The device according to claim 7, wherein the second beneficial agent is selected from a group consisting of paclitaxel, rapamycin, rapamycin derivatives, pimecrolimus, everolimus, fenofibrate, carvedilol, taxoteres, tacrolimus, butylated hydroxytoluene, butylated hydroxyanisole, vitamin E, danazol, probucol, tocopherols, tocotrienols, ABT-578, ABT-627 and analogs, derivatives, or combinations thereof.

9. The device according to claim 6, wherein the hydration inhibitor is associated with the first beneficial agent as a layer of the second beneficial agent at least partially covering the first beneficial agent.

10. The device according to claim 9, further comprising an outer layer of a third beneficial agent, the third beneficial agent having a third LogP value.

11. The device according to claim 10, wherein the third LogP value is less than the second LogP value.

12. The device according to claim 10, wherein the third beneficial agent is the same as the first beneficial agent.

13. The device according to claim 6, wherein the hydration inhibitor is associated with the first beneficial agent as a mixture of the second beneficial agent with the first beneficial agent.

14. The device according to claim 1, wherein the hydration inhibitor is associated with the beneficial agent as a mixture of the hydration inhibitor and the beneficial agent.

15. The device according to claim 14, wherein the hydration inhibitor is an additive.

16. The device according to claim 15, wherein the additive is selected from a group consisting of nitrophenyl octyl ether, bisethylhexyl sebacate, diisododecylphthalate, N-methylpyrrolidone, linolenic acid, linoleic acid, stearic acid, oleic acid, and combinations thereof.

17. The device according to claim 14, wherein the hydration inhibitor is a polymeric material.

18. The device according to claim 17, wherein the polymeric material is selected from a group consisting of phosphorylcholine, polycaprolactone, poly-D,L-lactic acid, poly-L-lactic acid, poly(lactide-co-glycolide), poly(hydroxybutyrate), poly(hydroxybutyrate-co-valerate), polydioxanone, polyorthoester, polyanhydride, poly(glycolic acid), poly(glycolic acid-co-trimethylene carbonate), polyphosphoester, polyphosphoester urethane, poly(amino acids), cyanoacrylates, poly(trimethylene carbonate), poly(iminocarbonate), polyalkylene oxalates, polyphosphazenes, polyiminocarbonates, and aliphatic polycarbonates, fibrin, fibrinogen, cellulose, starch, collagen, Parylene®, Parylast®, polyurethane, polycarbonate urethanes, polyethylene, polyethylene terephthalate, ethylene vinyl acetate, ethylene vinyl alcohol, silicone polysiloxanes, substituted polysiloxanes, polyethylene oxide, polybutylene terephthalate-co-PEG, PCL-co-PEG, PLA-co-PEG, polyacrylates, polyvinyl pyrrolidone, polyacrylamide, thermoplastic elastomers, polyolefin elastomers, EPDM rubbers, polyamide

elastomers, biostable plastic, acrylic polymers, nylon, polyesters, epoxies and derivatives or combination thereof.

19. The device according to claim 14, wherein the polymeric material has a  
5 zwitterionic pendant group.

20. The device according to claim 1, further comprising a layer of polymeric material  
on at least a portion of a surface of the interventional component, the beneficial agent at least  
partially loaded onto the layer of polymeric material.

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21. The device according to claim 20, wherein the layer of polymeric material has a  
zwitterionic pendant group.

22. The device according to claim 21. wherein the layer of polymeric material has a  
15 phosphoryl choline pendant group.

23. The device according to claim 20, wherein the hydration inhibitor controls a  
delivery of the beneficial agent from the layer of polymeric material.

20 24. The device according to claim 1, wherein the interventional component is  
selected from the group consisting of a stent, graft, stent-graft, valve, filter, coil, staple,  
suture, guidewire, catheter, and catheter balloon.

25 25. The device according to claim 1, wherein the first LogP value is at least about 0.5  
units less than the second LogP value.

26. A method of manufacturing a medical device, the method comprising the steps  
of:

30 providing an interventional component to be deployed in a patient;  
loading a beneficial agent on the interventional component for delivery therefrom, the  
beneficial agent having a first LogP value; and

associating an effective amount of a hydration inhibitor with the beneficial agent to control delivery of the beneficial agent from the interventional component, the hydration inhibitor having a second LogP value, the second LogP value being greater than the first LogP value.

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27. The method according to claim 26, wherein the beneficial agent loaded by the loading step is selected from a group consisting of antithrombotics, anticoagulants, antiplatelet agents, anti-lipid agents, thrombolytics, antiproliferatives, anti-inflammatories, agents that inhibit hyperplasia, smooth muscle cell inhibitors, antibiotics, growth factor  
10 inhibitors, cell adhesion inhibitors, cell adhesion promoters, antimetotics, antifibrins, antioxidants, antineoplastics, agents that promote endothelial cell recovery, antiallergic substances, viral vectors, nucleic acids, monoclonal antibodies, antisense compounds, oligonucleotides, cell permeation enhancers, pro-drugs and combinations thereof.

15 28. The method according to claim 27, wherein the beneficial agent loaded by the loading step is a nucleic acid, wherein the nucleic acid encodes a pharmaceutically useful peptide or an anti-sense oligo-nucleotide used to control a gene of interest in a cell of the patient.

20 29. The method according to claim 27, wherein the beneficial agent loaded by the loading step is selected from a group consisting indomethacin, phenyl salicylate, B-estradiol, vinblastine, ABT-627, testosterone, progesterone, paclitaxel, cyclosporin A, vincristine, carvedilol, vindesine, dipyridamole, methotrexate, folic acid, thrombospondin mimetics, estradiol, dexamethasone, metrizamide, iopamidol, iohexol, iopromide, iobitridol, iomeprol,  
25 iopentol, ioversol, ioxilan, iodixanol, iotrolan and pro-drugs, analogs, derivatives, or combinations thereof.

30 30. The method according to claim 26, wherein the hydration inhibitor associated by the associating step is selected from a group consisting of beneficial agents, polymeric materials, markers, additives, and combinations thereof.

31. The method according to claim 26, wherein the hydration inhibitor associated by the associating step is a second beneficial agent.

32. The method according to claim 31, wherein the second beneficial agent is  
5 selected from a group consisting of antioxidants, antithrombotics, anticoagulants, antiplatelet agents, anti-lipid agents, thrombolytics, antiproliferatives, anti-inflammatories, agents that inhibit hyperplasia, smooth muscle cell inhibitors, antibiotics, growth factor inhibitors, cell adhesion inhibitors, cell adhesion promoters, antimitotics, antifibrins, antioxidants, antineoplastics, agents that promote endothelial cell recovery, antiallergic substances, viral  
10 vectors, nucleic acids, monoclonal antibodies, antisense compounds, oligionucleotides, cell permeation enhancers, radiopaque agents markers and combinations thereof.

33. The method according to claim 32, wherein the second beneficial agent is selected from a group consisting of paclitaxel, rapamycin, rapamycin derivatives,  
15 pimecrolimus, everolimus, fenofibrate, carvedilol, taxoteres, tacrolimus, butylated hydroxytoluene, butylated hydroxyanisole, vitamin E, danazol, probucol, tocopherols, tocotrienols, ABT-578, ABT-627 and analogs, derivatives, or combinations thereof.

34. The method according to claim 26, wherein the associating step includes applying  
20 the second beneficial agent as a layer to at least partially cover the first beneficial agent.

35. The method according to claim 34, further comprising the step of applying a third layer of a third beneficial agent on at least a portion of the interventional component, the third beneficial agent having a third LogP value.  
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36. The method according to claim 35, wherein the third LogP value is greater than the second LogP value.

37. The method according to claim 36, wherein the third LogP value is the same as  
30 the first LogP value.

38. The method according to claim 34, wherein the associating step includes forming a mixture of the second beneficial agent with the first beneficial agent.

39. The method according to claim 26, wherein the associating step includes forming  
5 a mixture of the hydration inhibitor and the beneficial agent.

40. The method according to claim 39, wherein the hydration inhibitor associated by the associating step is an additive.

10 41. The method according to claim 40, wherein the additive is selected from a group consisting of nitrophenyl octyl ether, bisethylhexyl sebacate, diisododecylphthalate, N-methylpyrrolidone, linolenic acid, linoleic acid, stearic acid, oleic acid, and combinations thereof.

15 42. The method according to claim 39, wherein the hydration inhibitor associated by the association step is a polymeric material.

43. The method according to claim 42, wherein the polymeric material is selected from a group consisting of phosphorylcholine, polycaprolactone, poly-D,L-lactic acid, poly-L-lactic acid, poly(lactide-co-glycolide), poly(hydroxybutyrate), poly(hydroxybutyrate-co-valerate), polydioxanone, polyorthoester, polyanhydride, poly(glycolic acid), poly(glycolic acid-co-trimethylene carbonate), polyphosphoester, polyphosphoester urethane, poly(amino acids), cyanoacrylates, poly(trimethylene carbonate), poly(iminocarbonate), polyalkylene oxalates, polyphosphazenes, polyiminocarbonates, and aliphatic polycarbonates, fibrin,  
20 fibrinogen, cellulose, starch, collagen, Parylene®, Parylast®, polyurethane, polycarbonate urethanes, polyethylene, polyethylene terephthalate, ethylene vinyl acetate, ethylene vinyl alcohol, silicone polysiloxanes, substituted polysiloxanes, polyethylene oxide, polybutylene terephthalate-co-PEG, PCL-co-PEG, PLA-co-PEG, polyacrylates, polyvinyl pyrrolidone, polyacrylamide, thermoplastic elastomers, polyolefin elastomers, EPDM rubbers, polyamide  
25 elastomers, biostable plastic, acrylic polymers, nylon, polyesters, epoxies and derivatives or  
30 combination thereof.

44. The method according to claim 42, wherein the polymeric material has a zwitterionic pendant group.

5 45. The method according to claim 26, further comprising the step of applying a layer of polymeric material on at least a portion of a surface of the interventional component, and further wherein the loading step includes loading the beneficial agent at least partially onto the layer of polymeric material.

10 46. The method according to claim 45, wherein the layer of polymeric material applied by the applying step has a zwitterionic pendant group.

47. The method according to claim 46, wherein the layer of polymeric material applied by the applying step has a phosphoryl choline pendant group.

15 48. The method according to claim 45, wherein the hydration inhibitor associated by the associating step controls a delivery of the beneficial agent from the layer of polymeric material.

20 49. The method according to claim 26, wherein the interventional component is selected from the group consisting of a stent, graft, stent-graft, valve, filter, coil, staple, suture, guidewire, catheter, and catheter balloon.

25 50. The method according to claim 26, wherein the first LogP value of the beneficial agent loaded by the loading step is at least about 0.5 units less than the second LogP value of the hydration inhibitor associated by the associating step.

51. The method according to claim 26, wherein the effective amount of hydration inhibitor is an amount sufficient to shift the liquid-solid contact angle of the beneficial agent in association with the hydration inhibitor to at least 50°.

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52. The method according to claim 51, wherein the liquid-solid contact angle of the beneficial agent in association with the hydration inhibitor is at least about 70°.

53. A medical device comprising:

an interventional component to be deployed in a patient;

5 a beneficial agent to be delivered from the interventional component, the beneficial agent loaded on at least a portion of the interventional component and having a first LogP value; and

an effective amount of a hydration inhibitor associated with the beneficial agent to enhance the stability of a moisture sensitive beneficial agent from the interventional component, the hydration inhibitor having a second LogP value, the second LogP value being greater than the first LogP value.

54. The device according to claim 53, wherein the beneficial agent is selected from a group consisting of antithrombotics, anticoagulants, antiplatelet agents, anti-lipid agents, 15 thrombolytics, antiproliferatives, anti-inflammatories, agents that inhibit hyperplasia, smooth muscle cell inhibitors, antibiotics, growth factor inhibitors, cell adhesion inhibitors, cell adhesion promoters, antimetotics, antifibrins, antioxidants, antineoplastics, agents that promote endothelial cell recovery, antiallergic substances, viral vectors, nucleic acids, monoclonal antibodies, antisense compounds, oligonucleotides, cell permeation enhancers, 20 pro-drugs and combinations thereof.

55. The device according to claim 54, wherein the beneficial agent is selected from the group of indomethacin, phenyl salicylate,  $\beta$ -estradiol, vinblastine, ABT-627, testosterone, progesterone, paclitaxel, cyclosporin A, vincristine, carvedilol, vindesine, dipyridamole, 25 methotrexate, folic acid, thrombospondin mimetics, estradiol, dexamethasone, metrizamide, iopamidol, iohexol, iopromide, iobitridol, iomeprol, iopentol, ioversol, ioxilan, iodixanol, iotrolan and pro-drugs, analogs, derivatives, or combinations thereof.

56. The device according to claim 54, wherein the beneficial agent is a nucleic acid that 30 encodes a pharmaceutically useful peptide or an anti-sense oligo-nucleotide used to control a gene of interest in a cell of the patient.

57. The device according to claim 53, wherein the hydration inhibitor is selected from a group consisting of beneficial agents, polymeric materials, markers, additives, and combinations thereof.

5 58. The device according to claim 53, wherein the hydration inhibitor is a second beneficial agent.

59. The device according to claim 58, wherein the second beneficial agent is selected from a group consisting of antioxidants, antithrombotics, anticoagulants, antiplatelet agents, anti-lipid agents, thrombolytics, antiproliferatives, anti-inflammatories, agents that inhibit hyperplasia, smooth muscle cell inhibitors, antibiotics, growth factor inhibitors, cell adhesion inhibitors, cell adhesion promoters, antimitotics, antifibrins, antioxidants, antineoplastics, agents that promote endothelial cell recovery, antiallergic substances, viral vectors, nucleic acids, monoclonal antibodies, antisense compounds, oligonucleotides, cell permeation enhancers, radiopaque agents markers and combinations thereof.

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60. The device according to claim 59, wherein the second beneficial agent is selected from a group consisting of paclitaxel, rapamycin, rapamycin derivatives, pimecrolimus, everolimus, fenofibrate, carvedilol, taxoteres, tacrolimus, butylated hydroxytoluene, butylated hydroxyanisole, vitamin E, danazol, probucol, tocopherols, tocotrienols, ABT-578, ABT-627 and analogs, derivatives, or combinations thereof.

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